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ORIGINAL PAPER

Prevalence of non-infectious comorbidities in the HIV-positive population in Belgium: a multicenter, retrospective study

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ABSTRACT

Objectives: In Belgium, eleven AIDS Reference Centers (ARCs) and seven AIDS Reference Laboratories diagnose and treat HIV-positive individuals and track patients under care. As AIDS-related deaths are avoided and the HIV-positive population ages, non-infectious comorbidities (NICMs), such as cardiovascular disease, renal disease and certain cancers, play a larger role in the quality and length of patients' lives. This study aims to characterize the HIV-positive population in Belgium in terms of the prevalence of key NICMs.

Methods: We performed a retrospective study of 5787 HIV-positive patients under follow-up at four ARCs across Belgium between 1st of June 2014 and 1st of July 2016.

Results: The mean age of patients under follow-up was 46.7 (SD = 11.6) years, and the mean nadir CD4 count was 268.8 cells/mm^3 (SD = 189.5). The prevalence of diabetes mellitus, arterial hypertension and chronic kidney disease (CKD) were 5.9, 31 and 7.8%, respectively. Cardiovascular events, defined as the occurrence of myocardial infarction, stroke or an invasive coronary procedure, occurred in 2.9% of patients. The highest age-adjusted mortality rates were observed among patients 51–55 years of age. Mortality rates were also higher among patients with CKD and patients with viremic hepatitis C virus ($p < 0.05$).

Conclusions: Helping the aging HIV-positive population avoids premature morbidity and mortality from NICMs represents a key challenge to further improve patient outcomes. Belgium has an advanced system of HIV care and patient management; however, standardized data collection across ARCs is needed to improve knowledge sharing and to support future countrywide analyses.

KEYWORDS
HIV; AIDS; cohort studies; non-infectious comorbidities; Belgium

Introduction

The HIV epidemic has been transformed from an almost universally lethal viral disease to a chronic disease with near normal life expectancy, particularly in high-income countries [1–3]. In Belgium, a robust system of HIV patient tracking and care has been developed through the establishment of eleven AIDS reference centers (ARCs) and seven reference laboratories. A national analysis of the continuum of HIV care in Belgium from 2006 to 2008 found that 98.2% of diagnosed HIV individuals were linked to care and 90.8% were retained in HIV care [4]. In 2015, there were 15,266 HIV-infected patients under care at the 11 ARCs, with 2.7 new cases diagnosed per day [5].

As AIDS-related mortality has significantly declined through careful patient management and universal access to combination antiretroviral therapies (cART), physicians must consider the healthcare needs of the aging HIV-infected population. Multiple reviews of HIV-infected and healthy populations in high-income countries found that the mortality risk for aging HIV-infected patients with controlled viral load and CD4 counts greater than 500 is not necessarily higher than that of the general population [6,7]; however, there is evidence that HIV-infected patients may have a higher risk of developing non-infectious comorbidities (NICMs), including cardiovascular disease and kidney disease at a younger age than an age-matched uninfected population [3]. In a cross-sectional retrospective case–control study in Italy, there was a significantly greater NICM risk among HIV-infected patients than among matched controls. Additionally, the prevalence of NICMs among patients aged 41–50 years was similar to controls aged 51–60 years [8]. Age, sex, nadir CD4 count and ART

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Table 1. Patient characteristics in four AIDS reference centers (ARCs) in Belgium, 2014–2016.

	n (%)	SD
Follow-up	5787	
Mean age	46.7	11.6
Male gender	3609 (62.4%)	
On treatment[a]	4648 (95.3%)	
Region of origin		
Europe	2726 (47.1%)	
Sub-Saharan Africa	2452 (42.4%)	
Latin America/Caribbean	179 (3.1%)	
Asia	146 (2.5%)	
Other	284 (4.9%)	
CD4 count		
Mean recent CD4 (cells/mm^3)	566.2	280.1
<200	454 (8.3%)	
200–349	772 (14.1%)	
350–499	1173 (21.4%)	
500+	3126 (57.1%)	
Mean nadir CD4 (cells/mm^3)[b]	268.8	189.5
<200	1740 (39.0%)	
200–349	1528 (34.3%)	
350–499	722 (16.2%)	
500+	470 (10.5%)	
Other risk factors		
Smoking (former or current)[c]	1849 (39.9%)	
Hepatitis C RNA positive	164 (2.8%)	

[a]Only includes patients with known treatment status (n = 4880, 84.3% of sample).
[b]Only includes patients with known nadir CD4 (n = 4880, 84.3% of sample).
[c]Only includes patients with known smoking status (n = 4636, 80.1% of sample).

exposure were independent predictors of polypathology, or the simultaneous prevalence of two or more NICMs [8].

In recent years, the ARCs in Belgium have collected cohort data on patients under care. In this article, we synthesize the epidemiological data from four of these reference centers and present prevalence estimates of diabetes mellitus (DM), arterial hypertension (AT), cardiovascular events (CE), chronic kidney disease (CKD), anal cancer (AC), Hodgkin's Lymphoma (HL), lung cancer and liver cancer in the Belgian HIV-infected population. Additionally, mortality rates by age group are presented, as well as the prevalence rates of key NICMs in the patients who died during the study inclusion period.

Methods

Patient population

St. Pierre University Hospital, Brussels, Liège University Hospital, Ghent University Hospital, and Erasme University Hospital, Brussels, agreed to participate in the study. These centers provide care for approximately 40% of the HIV-positive patients in the country. Patients were included in the study if they received follow-up care at least once between 1 June 2014 and 1 July 2016. All patients under follow-up were assigned unique identification numbers to protect confidentiality and were included in the analysis. The study was approved separately by the ethical committees at all four centers.

Definitions of NICMs

The prevalence rates of NICMs in the living patient population under follow-up between 1 June 2014 and 1 July 2016 were determined using definitions based on the literature and constrained by available data.

CKD was defined as a confirmed estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 for patients with eGFR >60 mL/min/1.73 m^2 at baseline, or a confirmed 25% decline in eGFR for patients with eGFR <60 mL/min/1.73 m^2 at baseline [9].

CE was defined as the occurrence of myocardial infarction (MI), cerebrovascular accident, or invasive cardiovascular procedure (coronary artery bypass grafting, stenting). DM was defined as the clinical diagnosis of the condition or the prescription of antidiabetic drugs or insulin. Similarly, AT was defined as the clinical diagnosis of AT or the prescription of antihypertensive medication. HL, AC, lung cancer and liver cancer were determined by a diagnosis.

Polypathology was defined as concomitant diagnosis of more than one of the NICMs considered in this study (DM, CE, CKD, AT, HL, AC, lung cancer and liver cancer).

Statistical analysis

Analyses were performed with R Statistical Software version 3.2.2 [10].

Only deaths that occurred between 1 June 2014, and 1 July 2016 were considered in the mortality calculations. Deaths from any cause were included. Age-adjusted mortality rates were calculated using the combined population and deaths in each five-year age group of the four centers.

The relationship between categorical variables was assessed using Fisher's exact test and odds ratios. A p-value < 0.05 was considered significant.

Results

There were 5787 living patients under regular care in the four AIDS References Centers which were included in this study, of which 37.6% were female. Mean age was 46.7 years (SD = 11.6 years) and almost 40% of the population was over the age of 50; 47.1% were from European origin, 42.4% were from sub-Saharan Africa, and 3.1% were from Latin America and the Caribbean (Table 1).

Treatment rates were high, with 95.3% of patients under follow-up on cART. The most recent CD4 count during follow-up was an average of 566.2 cells/mm^3 (SD = 280.1). Reflecting the high treatment rates in the centers, 57.1% of patients had a recent CD4 count above 500 cells/mm^3, while 21.4% had a count between 350 and 499, 14.1% between 200 and 349, and 8.3% under 200.

Patients had an average nadir CD4 count of 268.8 cells/mm^3 (SD = 189.5). The proportion of patients with

Table 2. Prevalence of non-infectious comorbidities (NICMs) in four AIDS reference centers (ARCs) in Belgium, 2014–2016.

NICM	All ages ($n = 5787$) (%)	≤40 years ($n = 1833$) (%)	41–50 years ($n = 1824$) (%)	51–60 years ($n = 1433$) (%)	>60 years ($n = 695$) (%)
Diabetes mellitus	5.9	1.8	4.5	10.1	12.2
Arterial hypertension	31.0	16.5	30.2	43.7	45.2
Cardiovascular events[a]	2.9	0.6	1.3	5.1	8.0
Chronic kidney disease	7.8	1.8	5.2	10.6	24.8
Anal cancer	0.3	0.2	0.2	0.7	0.4
Hodgkin's lymphoma	0.5	0.2	0.4	0.9	0.6
Lung cancer	0.1	0	0.1	0.3	0
Liver cancer	0.1	0	0	0.1	0.1
Polypathology	8.9	2.1	5.3	14.6	24.5

[a]Only includes patients for whom data on CE was available ($n = 4880$, 84% of sample).

Table 3. Differences in mortality among patients with or without DM, CE, CKD, HCV, or polypathology 2014–2016.

NICM or risk factor	Prevalence – living patients ($n = 5787$) (%)	Prevalence – deceased patients ($n = 31$) (%)	OR	95% CI	*p* value
Diabetes mellitus	5.9	12.9	2.3	0.6–6.8	0.1110
Arterial hypertension	31.0	16.1	0.4	0.1–1.1	0.0811
Cardiovascular events[a]	2.9	8.0	2.9	0.3–11.9	0.1660
Chronic kidney disease	7.7	22.6	3.5	1.3–8.4	0.0085**
Hepatitis C virus	2.8	16.1	6.6	2.0–17.7	0.0018**
Polypathology	8.9	19.4	2.5	0.8–6.2	0.0541

[a]Only includes patients for whom data on CE was available ($n = 4880$, 84% of sample).
**indicates significance at the $p < 0.05$ level.

a nadir CD4 count below 200 cells/mm^3 was 39.0%, and the proportion between 200 and 350 was 34.3%. The remaining 26.7% of patients had a nadir CD4 count above 350. To consider other risk factors, just under 40% of patients with known smoking status ($n = 4636$, 80.1% of sample) were current or former smokers, and 2.8% were chronically coinfected with hepatitis C virus (HCV) (Table 1).

Prevalence of NICMs

Prevalence rates by age group are listed in Table 2. Prevalence rates of key NICMs increased by age group, with a steep increase in the 51–60-year age group and the over 60 age group. The prevalence rates of HL and AC were higher in the 51–60-year olds than in patients older than 60. Of note, almost 11% of patients 51–60 years old and 25% of patients 60 and older had CKD. Similarly, the prevalence of CE jumped from 1.3% in the 41–50-year-old age group to 5.1% in 51–60 years and 8.0% in patients 60 and older. Rates of polypathology reached 24.5% in the over 60 age group.

Mortality

Mortality rates were calculated by age group. Overall, there were 31 deaths during the study period. Of these, 32% occurred in patients aged 51–55, for whom the age-adjusted mortality rate was 12 deaths per 1000 patients. The group with the second highest mortality rate was in patients aged 26–30, with a rate of 9 deaths per 1000 patients.

The prevalence estimates in living patients and patients who died during the study inclusion period with a diagnosis of at least one NICM were compared (Table 3). In the deceased patient population, the prevalence of CKD was 22.6%, while the prevalence of CE was 12%. Patients with CKD had 3.5 (95% CI: 1.2–8.3) times the risk of death during the study period compared to patients without CKD ($p < 0.05$). There was no significant difference in risk of death between patients who had been diagnosed with DM, AT or CE. Anal cancer, lung cancer, liver cancer and HL were not considered due to the small number of cases in both living and deceased patients. HCV-RNA-positive patients had 6.6 (95% CI: 2.0–17.7) times the risk of death during the study period than patients without HCV.

Discussion

This cross-sectional, retrospective analysis of cohort data from four Belgian HIV reference centers provides a summary of patient characteristics and mortality risk factors. Additionally, this study represents the first multicenter analysis in Belgium that provides age-stratified prevalence rates of key NICMs in the aging HIV-positive population. Almost 40% of the infected population in the four centers was 50 years or older in 2015. The prevalence rates of CKD, DM, AC and HL were the highest in the 51–60-year-old population, and most deaths occurred among patients aged 51–55. Prevalence and the advancement of NICMs may continue to rise as the HIV-positive population ages. Furthermore, the significantly higher risk of mortality among patients coinfected with HCV, though not unexpected, underscores the importance of access to antiviral therapies for HCV for eligible patients when possible. These findings highlight a need for prudent patient management to avoid premature morbidity and mortality from NICMs in addition to the management of patients' antiretroviral regimens.

Almost 40% of patients had a nadir CD4 count under 200 cells/mm^3, potentially putting them at greater risk for the development of NICMs. There is evidence that low nadir CD4 counts and declining CD4 counts are associated with a greater risk of some NICMs and death [11,12]. Strategies to improve testing among high-risk groups in Belgium are needed to reduce the number of late presenters, or patients who have a CD4 count of less than 350 cells/mm^3 at diagnosis [13]. In addition to the integration of comorbidity prevention and monitoring into the standard of care for patients, improving rates of early diagnosis and cART initiation may lower the incidence of NICMs among the HIV-positive population.

There were some limitations due to the historical data that were collected in each of the four centers. One of the major takeaways from the analysis was the need for standardized definitions of risk factors and comorbidities to strengthen data collection in the ARCs. For example, the definition of CE as MI, cerebrovascular accident, or invasive cardiovascular procedure (coronary artery bypass grafting, stenting) did not include fatal MI or fatal stroke because patients' causes of death were not systemically recorded in all centers. This could explain the lack of significant association between CE and death in this analysis. The definition of CKD, though originally from a published study, may be an overestimation of the condition due to the inhibition of creatinine excretion, and therefore, artificial increase in creatinine blood levels, induced by certain widely used medications in the treatment of HIV, diabetes and hypertension.

Additionally, the recording of tobacco use and body mass index was not consistent between centers. The prevalence of tobacco smoking or historical smoking was measured through self-reported rates of smoking. Data on cessation rates for patients who have ever smoked were not available in all centers; thus, a positive response indicates that the patient has previously been or still is a smoker. These data may underestimate the rates of smoking in the population due to underreporting by either the patient or practicing physician. Despite possible underreporting, almost half of the patients were past or present smokers, which may contribute to the development of NICMs among patients.

In conclusion, Belgium has an advanced system of HIV patient care and tracking in place in 11 ARCs across the country. However, this study represents the first multicenter data analysis focusing on the prevalence rates of key NICMs and risk factors in the HIV-positive population. This study highlights the need for standardized data collection to allow uniform risk factor and NICM definitions at the national level to make countrywide analyses possible. The data collection methodology used in this study could be expanded to include all eleven reference centers and used to initiate prospective surveillance as the foundation for predictive modeling efforts to address NICMs in the HIV-positive population.

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References

[1] Matic SL, JV, Donoghoe, MC. HIV/AIDS in Eruope – Moving from death sentence to chronic disease management. WHO, editor. WHO; 2006.
[2] Mocroft A, Reiss P, Rakhmanova A, et al. A survey of ATRIPLA use in clinical practice as first-line therapy in HIV-positive persons in Europe. Infection. 2014;42(4):757–762.
[3] Smit M, Brinkman K, Geerlings S, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. Lancet Infect Dis. 2015;15(7):810–818.
[4] Van Beckhoven D, Buve A, Ruelle J, et al. Belgian HIVCSG. A national cohort of HIV-infected patients in Belgium: design and main characteristics. Acta Clin Belg. 2012;67(5):333–337.
[5] Institut scientifique de Santé publique (WIV-ISP). Épidémiologie du SIDA et de l'infection à VIH en Belgique. 2016.
[6] Costagliola D. Demographics of HIV and aging. Curr Opin HIV AIDS. 2014;9(4):294–301.
[7] Sabin CA. Do people with HIV infection have a normal life expectancy in the era of combination antiretroviral therapy? BMC Med. 2013;11(1):251.
[8] Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clin Infect Dis. 2011;53(11):1120–1126.
[9] Mocroft A, Kirk O, Reiss P, et al. Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients. AIDS. 2010;24(11):1667–1678.
[10] R Development Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2015.
[11] Silverberg MJ, Leyden WA, Xu L, et al. Immunodeficiency and risk of myocardial infarction among HIV-positive individuals with access to care. J Acquir Immune Defic Syndr. 2014;65(2):160–166.
[12] Helleberg M, Kronborg G, Larsen CS, et al. CD4 decline is associated with increased risk of cardiovascular disease, cancer, and death in virally suppressed patients with HIV. Clin Infect Dis. 2013;57(2):314–321.
[13] Yombi JC, Jonckheere S, Vincent A, et al. Late presentation for human immunodeficiency virus HIV diagnosis results of a Belgian single centre. Acta Clin Belg. 2014;69(1):33–39.